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10/582,761

06/13/2006

Bengt Langstrom

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GE HEALTHCARE, INC.

IP DEPARTMENT 101 CARNEGIE CENTER

PRINCETON, NJ 08540-6231

EXAMINER

SCHLIENTZ, LEAH H

ART UNIT

PAPER NUMBER

1618

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DELIVERY MODE

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

| | | | |
|------------------------------|--------------------------------------|---|--|
| Office Action Summary | Application No. 10/582,761 | Applicant(s) LANGSTROM ET AL. | |
| | Examiner Leah Schlientz | Art Unit 1618 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 31 August 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-23 is/are pending in the application.
- 4a) Of the above claim(s) 10 and 12-23 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-9 and 11 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 13 June 2006 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date <u>2/6/2008 and 6/13/2006</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I, claims 1-17, in the reply filed on 4/30/2009 is acknowledged. The traversal is on the ground(s) that the compounds disclosed in the kit claim 18 are disclosed in the method claim 9, and the claims do not lack the same technical features and the Examiner would not be presented with an undue burden to search claims 1-23. This is not found to be persuasive. The common technical feature between claims 9 and 23 (i.e. compounds of claim 23) are not a "special" technical feature because the compounds of claim 23 are known in the art. See for example Steel et al., Appl. Radiation and Isotopes, 1999, 51, p. 377 - 388, disclosing ^{11}C urea. Therefore, since the common technical feature (i.e. labeled compounds such as ^{11}C urea) do not make a contribution over the prior art, the common technical feature cannot be a "special" technical feature, and lack of unity has been established. See MPEP 1893.03(d). The requirement is still deemed proper and is therefore made FINAL.

The election of species of reagent, azide and labeled compound in the reply filed 8/31/2009 are also acknowledged. However, in response to a telephone call placed by the examiner to Craig Bohlken on 12/7/2009 to clarify the election of species, the examiner was informed that the species that Applicant would like to elect correspond to the first reagent listed in claim 8, and the first labeled compound listed in claim 9. Accordingly, for the purpose of preliminary prior art search the elected species are

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considered to be R'R''NH as reagent, R'N₃ as azide and R-NH-C(=O)-NR'R'' as labeled compound.

Status of Claims

Claims 1-23 are pending, of which claims 18-23 are withdrawn from consideration at this time as being drawn to a non-elected invention. Claims 10 and 12-17 are withdrawn from consideration as being drawn to non-elected species. Claims 1-9 and 11 are readable upon the elected invention and are examined herein on the merits for patentability.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-9 and 11 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over the claims of copending Application No. 11/086,632. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to a method for labeling synthesis comprising providing a high pressure chamber with a liquid inlet and a gas inlet, providing an azide solution mixed with a transition metal complex and a reagent, introducing carbon-isotope enriched gas, reacting and collecting product. Accordingly, the claims are overlapping in scope and are obvious variants of one another.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-7 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of labeling synthesis of the compounds of claim 9 comprising performing the reaction steps recited in claim 1, wherein the appropriate reagent is selected from those listed in claim 8, it does not reasonably provide enablement for a method of labeling synthesis of any "labeled compound" comprising performing the steps of claim 1 by providing an azide solution to be labeled

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mixed with a transition metal complex and any "appropriate reagent," as broadly claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

- 1) the quantity of experimentation necessary,
- 2) the amount of direction or guidance provided,
- 3) the presence or absence of working examples,
- 4) the nature of the invention,
- 5) the state of the prior art,
- 6) the relative skill of those in the art,
- 7) the predictability of the art, and
- 8) the breadth of the claims.

The instant specification fails to provide guidance that would allow the skilled artisan to practice the instant invention without resorting to undue experimentation, as discussed in the subsections set forth herein below.

The nature of the invention and the breadth of the claims

The nature of the invention is a method for labeling synthesis comprising (a) providing a high pressure reaction chamber having a liquid inlet and a gas inlet in a bottom surface thereof, (b) providing an azide solution to be labeled mixed with a transition metal complex and an appropriate reagent, (c) introducing a carbon-isotope monoxide enriched gas mixture into the reaction chamber via the gas inlet, (d) introducing at high pressure said azide solution mixed with transition metal complex and

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other reagents into the reaction chamber via the liquid inlet, (e) waiting for a predetermined time while the labeling synthesis occurs, and (f) collecting the labeled compound from the reaction chamber. The claims are broad and are inclusive of any and all "appropriate reagents" and "labeled compounds."

The state of the prior art, the relative skill of those in the art, and the predictability of the art

The art is developed with regard to the reaction of azide and carbon monoxide in the presence of transition metal catalyst with regard to certain reagents and products. For example, the synthesis of isocyanate, carbamates, ureas, etc. are known by such reaction as shown by Dickson (*Homogeneous Catalysis with Compounds of Rhodium and Iridium*, 1985, Springer, p. 135-137). However, based on the almost unlimited number of further potential reagents or compounds available to the organic chemist, having an almost unlimited number and orientation of functional groups which may react in the presence of azide and carbon monoxide, there would be some degree of unpredictability as to reactions which may successfully take place with reagents other than those disclosed in claim 8, and which products may form other than those disclosed in claim 9.

The amount of direction provided, the presence of working examples, and the quantity of experimentation necessary

The specification provides direction regarding the reactions performed between azides and amines, alcohols, thiols, Grignard reagents, unsaturated hydrocarbons, etc. on pages 21-22 of the instant specification, and the production of carbamides,

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carbamates, thiocarbamates, amides, lactams, oxazolidones, etc. on pages 21-22 of the instant specification. Specific examples of the preparation of diphenylurea, ethylphenylcarbamate, acetoanilide, oxazolidone are provided. However, based on such a limited disclosure of a few specific reagents and labeled products which may be produced by the claimed method, a great deal of experimentation would be necessary in order for the skilled artisan to extrapolate the claimed method to include synthesis of any labeled compound using any reagent, based on the almost unlimited number of potential reagents and compounds, and their almost unlimited number and potential orientation of functional groups on such molecules. Accordingly, the claims are more broad than the enabling disclosure.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or non

Claims 1-9 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dickson (*Homogeneous Catalysis with Compounds of Rhodium and Iridium*, 1985, Springer, p. 135-137), in view of Kihlberg *et al.* (*J. Org. Chem.*, 2002, 67, p. 3687-92), in further view of Kihlberg *et al.* (WO 02/102711).

Dickson discloses that the carbonylation of azides such as PhN_3 provides a route to isocyanates in the presence of rhodium catalysts, or that in the presence of EtOH or PhNH_2 , the products of the carbonylation reaction are PhNHCO_2Et (carbamate) and PhNHCONHPh (carbamide or urea derivatives), respectively. 1,3-Diarylsureas are also obtained by the reductive carbonylation of arylazides with CO and H_2 in the presence of $\text{Rh}_6(\text{CO})_{16}$ as catalyst (pages 135, last paragraph -136). Carbonylation of amines is also disclosed for the synthesis of ureas (pages 136-137).

Dickson does not specifically teach performing the reaction using ^{11}C labeled carbon monoxide using a high pressure reaction chamber. It is for this reason that Kihlberg (2002) and Kihlberg '711 are joined.

Kihlberg (2002) discloses using amines, amino alcohols, or alcohols in selenium-mediated synthesis with $[^{11}\text{C}]$ carbon monoxide in the synthesis of ureas, carbamates and carbonates (abstract). Kihlberg teaches that carbamoyl groups are common biologically active compounds such as pharmaceuticals and are an important target for ^{11}C labeling (page 3687, left column). A crucial step in labeling methods using $[^{11}\text{C}]$ carbon monoxide was the advent of a method that makes it possible to efficiently use ^{11}C carbon monoxide in labeling synthesis, e.g. a fully automated method, where ^{11}C

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carbon monoxide is concentrated to a volume of 10-50 μL , transferred to a microautoclave and pressurized with the reaction mixture at 30-40 kPa (page 3687-8). See schemes 1 and 2. The use of ^{11}C carbon monoxide at concentrations below 10^{-4} M in selenium-promoted carbonylations of amines, alcohols and amino alcohols has been shown to be a viable method for the production of carbamoyl compounds. The method is rapid, mild, and conducted in a one-pot procedure using an automated apparatus. This apparatus has become commercially available is useful for a range of other carbonylation reactions. The method holds promise for routine production of ^{11}C labeled compounds (page 3690, right column).

Kilhberg '711 teaches a method and apparatus for production and use of ^{11}C carbon monoxide in labeling synthesis (title). ^{11}C carbon monoxide enriched gas is produced from an initial ^{11}C carbon dioxide gas mixture (page 1, lines 1-8). The labeling synthesis occurs as follows (page 6):

- Providing a high-pressure reaction chamber having a liquid reagent inlet and a labeling reactant inlet in a bottom surface thereof.
- Providing a liquid reagent volume that is to be labeled.
- Introducing the carbon-isotope monoxide enriched gas-mixture into the reaction chamber via the labeling reactant inlet.
- Introducing, at high pressure, said liquid reagent into the reaction chamber via the liquid reagent inlet.
- Waiting a predetermined time while the labeling synthesis occurs.
- Removing the labeled liquid reagent from the reaction chamber.

The carbon-isotope monoxide enriched gas mixture is produced by (page 5):

- Providing carbon-isotope dioxide with a suitable carrier gas.
- Converting carbon-isotope dioxide to carbon-isotope monoxide by introducing said gas mixture in a reactor device.
- Removing traces of carbon-isotope dioxide by flooding the converted gas-mixture through a carbon dioxide removal device wherein carbon-isotope dioxide is trapped but not carbon-isotope monoxide nor the carrier gas.

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- Trapping carbon-isotope monoxide in a carbon monoxide trapping device, wherein carbon-isotope monoxide is trapped but not said carrier gas.
- Releasing said trapped carbon-isotope monoxide from said trapping device, whereby a volume of carbon-isotope monoxide enriched gas-mixture is achieved.

The final pressure of the liquid in the reaction chamber is approximately 80 times higher than the original gas pressure, thus a pseudo one-phase system results (page 11, lines 1-10). Advantages achieved by the apparatus and methods are that the resulting labeled compound is highly concentrated, and that the miniaturization of the synthesis system facilitates automation, rapid synthesis and purification, and optimization of specific radioactivity through minimization of isotopic dilution. Most important is the opening of completely new synthesis possibilities (page 4).

It would have been obvious to one of ordinary skill in the art to perform labeling of carbamoyl compounds by performing carbonylation reactions using azide and reagents such as amine or alcohol using ^{11}C carbon monoxide in an automated reactor, when the teaching of Dickson is taken in view of Kilhberg (2002) and Kilhberg '711. Dickson teaches that carbamoyl products, such as ureas, can be synthesized via carbonylation of azide or amines, but does not specifically recite ^{11}C labeling. However, Kilhberg (2002) teaches ^{11}C carbonylation via carbon monoxide of amines to prepare ureas and carbamates, and teaches that carbamoyl groups are an important target for ^{11}C -labeling. Accordingly, one would have been motivated to perform the carbamoyl synthesis reactions using azide, as in Dickson, using ^{11}C labeled carbon monoxide because Kilhberg (2002) teaches that carbamoyl compounds are important targets for ^{11}C labelling, and because the automated synthesis methods and apparatus (e.g. such as that disclosed in Kihlberg '711) have advantages such as being rapid, mild, and

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conducted in a one-pot procedure using an automated apparatus. The apparatus has become commercially available is useful for a range of other carbonylation reactions. The method holds promise for routine production of ^{11}C labeled compounds (page 3690, right column). Kihlberg also teaches that the device of the '711 document can be used for ^{11}C carbon monoxide synthesis of ureas, carbamates, etc. (page 16).

Conclusion

No claims are allowed at this time.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leah Schlientz whose telephone number is 571-272-9928. The examiner can normally be reached on Monday - Friday 8 AM - 5 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael G. Hartley/
Supervisory Patent Examiner, Art Unit 1618

LHS